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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Snow et al.  
Appl. No. : 09/544,344  
Filed : April 6, 2000  
Title : MATERIALS, METHOD AND APPARATUS FOR DETECTION AND  
MONITORING OF CHEMICAL SPECIES  
Art Unit : 1743  
Examiner : Arlen Soderquist

Honorable Commissioner for Patents  
Washington, DC 20231

**APPEAL BRIEF**

Sir:

The present appeal is taken from the final rejection dated November 7, 2002, of claims 1 through 9 and 21-36 (all presently pending claims) of the above-identified application. The claims on appeal appear in the attached APPENDIX.

**I. REAL PARTIES IN INTEREST**

The real parties in interest are the United States Government, as represented by the Secretary of the Navy, and MicroSensor Systems, Inc.

**II. RELATED APPEALS AND INTERFERENCES**

Appellants are unaware of any other appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**III. STATUS OF CLAIMS**

Claims 1 through 9 and 21-36, the only claims currently pending, have been finally rejected and are the claims on appeal. Claims 10 through 20 allowed and issued in U.S. Patent No. 6,221,673.

#### IV. STATUS OF AMENDMENTS

No amendment was filed or proposed after final rejection.

#### V. SUMMARY OF THE INVENTION

The present invention relates to the detection or quantitation of a chemical species in a target environment, and the discovery that the properties of certain particles, which are interactive with the chemical species, can advantageously be monitored as an indication or in what amount the species is present.

As stated on page 5, lines 12-22, one aspect of the invention is an article of manufacture suitable for use in determining whether or in what amount a chemical species is present in a target environment, which article comprises a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and on said core a ligand shell, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered.

As stated on page 13, lines 12-17, the ligand shell is advantageously neither so thin that the multiplicity of particles is effectively metallic in its conductivity properties, nor so thick that the multiplicity of particles is completely electrically insulating. Preferably, such thickness ranges from 0.4 to 4 nm, especially 0.4 to 2.5 nm.

#### VI. ISSUES

A. Are claims 1-5, 7-9, 21-26, and 33-34 anticipated by Bethell (*J. Electroanal. Chem.* 409 (1996) 137-143) under 35 U.S.C. § 102(b)?

B. Are claims 2, 4, 6, and 22 obvious under 35 U.S.C. § 103(a) over Bethell (*J. Electroanal. Chem.* 409 (1996) 137-143) in view of U.S. Patent 5,609,907 to Natan?

C. Are claims 27-32 and 35-56 obvious under 35 U.S.C. § 103(a) over Bethell (*J. Electroanal. Chem.* 409 (1996) 137-143) in view of Terrill (*J. Am. Chem. Soc.* 1995, 117, 12537-12548)?

## VII. GROUPING OF CLAIMS

Applicants urge that each of the rejected claims stands on its own recitation, the claims considered to be separately patentable.

## VIII. ARGUMENT

A. Claims 1-5, 7-9, 21-26, and 33-34 define subject matter that is patentable over Bethell.

To be anticipating, a reference must disclose every element of the claims. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989). If the reference lacks any claimed element, there is no anticipation. *Kloster Speedsteel AB v. Crucible Inc.*, 793 F.2d 1565, 1571 (Fed. Cir. 1986).

According to the specification (page 13, lines 12-17), “[t]he shell is advantageously neither so thin that the multiplicity of particles is effectively metallic in its conductivity properties, nor so thick that the multiplicity of particles is completely electrically insulating. Preferably, such thickness ranges from 0.4 to 4 nm, especially 0.4 to 2.5 nm.” Independent claims 1, 21, 25, 33 and 34 each contain as an element, a ligand shell “of thickness from 0.4 to 4.0 nm.” Bethell only describes using dithiols with bare clusters to make three-dimensional networks. Although Bethell discusses particle core size, Bethell does not teach or disclose

particles with a ligand shell of the required thickness. Therefore, Bethell does not anticipate claims 1-5, 7-9, 21-26, and 33-34.

Moreover, Bethell's disclosure is not an electrical configuration for a sensing device and does not teach or disclose an article of manufacture, an assembly, or a system suitable for use in determining whether or in what amount a chemical species is present in a target environment, as recited in the preamble of independent claims 1, 21, 25, 33 and 34. Language of the preamble is legally limiting if it is essential to point out the invention defined by the claims. *See Perkin-Elmer Corp. v. Computervision Corp.*, 732 F.2d 888 (Fed. Cir. 1984). One way to make the preamble legally limiting is to expressly incorporate by reference the preamble phrase. *See Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 55 F.3d 615 (Fed. Cir. 1995). In *Bell Communications Research*, the court held that "These two steps of the claimed method, by referring to 'said packet,' expressly incorporate by reference the preamble phrase 'said packet including a source address and a destination address.'" In the present application, the independent claims incorporate by reference determining "whether or in what amount a chemical species is present in a target environment" by referring to "said species" in the body of the claim.

The objective of Bethell "was to develop materials in which it would be possible to control the transfer of electrons from one metal particle to another by controlling the size of the particles, their separation and, we hoped, the chemical nature of the organic spacers providing that separation. We had in mind particularly the possibility that, by incorporating into the spacers organic moieties that could be addressed electrochemically or photochemically, we could go some way towards the construction of electronic circuitry of a size range approaching the molecular." (Page 409, col. 1-2) The focus of Bethell is on using only dithiols to link large bare clusters together for electronic circuitry. Throughout the reference, Bethell stays focused on its

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objective and in no way infers, speculates, or provides any means for anticipating that metal (gold or otherwise) nanoparticles with an appropriate ligand shell could be used for chemical detection as described in the claims of the present application. In fact, in the last paragraph of the conclusion, Bethell speculates that “there are many applications for the nanostructured materials that have been described here. These range from submicroelectronic devices and circuitry (switches, diodes, electrochromics and photovoltaics) to electrical modification of the reflectance of glass.” Chemical sensors are not included in Bethell’s range of applications, and the configuration of this range of devices is not what one of ordinary skill in the art would select for a chemical sensor. Bethell does not teach or disclose a chemical sensor application as recited in the claims of the present application. Therefore, Bethell does not anticipate claims 1-5, 7-9, 21-26, and 33-34.

B. Claims 2, 4, 6, and 22 define subject matter that is patentable over Bethell in view of Natan.

To establish a prima facie case of obviousness, the Examiner must show that one of ordinary skill in the art would have been motivated by the prior art to fashion an embodiment satisfying all claim limitations. *In re Royka*, 490 F.2d 981 (C.C.P.A. 1974); M.P.E.P. 2143.03.

Like Bethell (as discussed above in section A of the Argument), Natan fails to disclose a ligand shell with a thickness from 0.4 to 4 nm. The assemblies disclosed in Natan use large bare gold clusters that physisorb proteins such as streptavidin to achieve the non-covalent attachment of metal core particles. The proteins are very large molecules and, if used to coat a metal particle, would generate a shell so thick that each particle would be insulated from another and electron transport would not be measurable. Therefore, the hypothetical combination of Bethell and Natan does not disclose every claim limitation and, thus, does not render obvious claims 2,4, 6 and 22.

Moreover, like Bethell (as discussed above in section A of the Argument), Natan does not disclose an article of manufacture or an assembly for use in determining whether or in what amount a chemical species is present in a target environment. The scope of Natan is limited to the preparation of self-assembled metal colloids as monolayer depositions primarily for the purpose of surface enhanced Raman spectroscopy (SERS) analytical applications. In Natan's abstract, other applications are suggested (e.g., biocompatible surfaces, catalysts, nonlinear optics and electrochemical applications), but all prescriptions for depositions of metal colloids use bare gold clusters and conform with a procedure dedicated to the SERS application. The scope and content of the art described in Natan is focused on the SERS application, which allows for optical sensing but not electronic sensing, and cannot accommodate an extension to a chemical sensing application as recited in the claims of the present invention. Therefore, the hypothetical combination of Bethell and Natan does not render obvious claims 2, 4, 6 and 22.

C. Claims 27-32 and 35-36 define subject matter that is patentable over Bethell in view of Terrill.

Like Bethell (as discussed above in section A of the Argument), Terrill fails to disclose a ligand shell with a thickness from 0.4 to 4 nm as required by claims 27-32 and 35-36. In Terrill, electrical conductivity measurements were made using very thick coatings. The coating deposition method of Terrill is a drop casting technique using a solution with a 100 mg/mL concentration that produces coatings of 2-20  $\mu\text{m}$  thick, which is many times thicker than the height of the electrode. (Terrill last paragraph on page 2538) In the present application, it is explicitly stated that this technique is not adequate for a chemical sensing application and that acceptable "thin" film deposition techniques include spraying fine mist of a dilute solution onto a preferably heated substrate surface and chemical self assembly. (Page 17, line 8 through page

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19, line 2) Therefore, the hypothetical combination of Bethell and Natan does not disclose every claim limitation and, thus, does not render obvious claims 27-32 and 35-36.

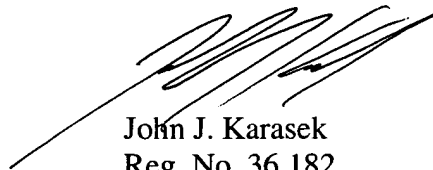
Moreover, like Bethell (as discussed above in section A of the Argument), Terrill does not teach "connecting said pair of electrodes with a sensor capable of determining a change in the property of said multiplicity of particles," as required by claims 27-32, and "means for monitoring the electrical resistivity of said multiplicity of particles to determine whether there is, or the amount of, any change in said resistivity as an indication of whether or in what amount said species is present," as required by claims 35-36. The electrical conductivity measurements in Terrill were made in a vacuum, which shows no anticipation of a sensor application. Therefore, the hypothetical combination of Bethell and Natan does not render obvious claims 27-32 and 35-36.

#### IX. CONCLUSION

For the reasons stated above, Applicants respectfully request reversal of the rejections under 35 U.S.C. §§ 102(b) and 103(a).

Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 50-0281.

Respectfully submitted,



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**APPENDIX – The claims on appeal**

1. An article of manufacture suitable for use in determining whether or in what amount a chemical species is present in a target environment, which article comprises a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and on said core a ligand shell, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered.
2. An article of manufacture as defined in claim 1, wherein said core comprises silver, gold, platinum or palladium, or an alloy of two or more such metals.
3. An article of manufacture as defined in claim 1, wherein said ligand shell comprises a substance which is capable of interacting with said species such that the conductivity of said multiplicity of particles is altered.
4. An article of manufacture as defined in claim 1, wherein said ligand shell comprises a thiol or an amine.
5. An article of manufacture as defined in claim 4, wherein said ligand shell comprises a thiol selected from the group consisting of primary aliphatic thiols, secondary aliphatic thiols, tertiary aliphatic thiols, heterofunctionally substituted aliphatic thiols, aromatic thiols, heterofunctionally substituted aromatic thiols, and heterofunctionally substituted araliphatic thiols.
6. An article of manufacture as defined in claim 4, wherein said ligand shell comprises an amine selected from the group consisting of primary aliphatic amines.

7. An article of manufacture as defined in claim 1, wherein in each said particle the core is of size from 2 to 20 nm in maximum dimension and the ligand shell is of thickness from 0.4 to 2.5 nm.

8. An article of manufacture as defined in claim 1, wherein the particles are substantially spherical.

9. An article of manufacture as defined in claim 1, wherein the ligand contains a heterofunctional group capable of binding both with the core and the analyte of interest.

21. An assembly suitable for investigation of a target environment to determine whether or in what amount a chemical species may be present, which comprises

(a) a substrate suitably configured for presenting a multiplicity of particles supported thereon to contact with said environment;

(b) supported by said substrate, a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered; and

(c) a sensor for monitoring said property of said multiplicity of particles.

22. An assembly as defined in claim 21, wherein said core comprises silver, gold, platinum or palladium or an alloy of two or more of such metals.

23. An assembly as defined in claim 21, wherein said core comprises silver, gold, platinum or palladium or an alloy of two or more of such metals.

24. An assembly as defined in claim 21, wherein the film is of thickness from 5 to 10,000 nm.

25. An assembly suitable for investigating a target environment, to determine whether or in what amount a chemical species may be present, which comprises

- (a) a substrate suitably configured for presenting a multiplicity of particles supported thereon to contact with said species;
- (b) supported by said substrate, said multiplicity of particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that the electrical conductivity of particles is altered;
- (c) a pair of electrodes, each in electrical contact with said multiplicity of particles; and
- (d) a sensor for monitoring the electrical conductivity of said multiplicity of particles to determine whether there is, or the amount of, any change in said conductivity as an indication of whether or in what amount said species is present.

26. An assembly as defined in claim 25, wherein the core comprises gold and the ligand is selected from the group consisting of primary aliphatic thiols, secondary aliphatic thiols, tertiary aliphatic thiols, heterofunctionally substituted aliphatic thiols, aromatic thiols, heterofunctionally substituted aromatic thiols, and heterofunctionally substituted araliphatic thiols.

27. A method of fabricating an assembly suitable for investigation of a target environment to determine whether or in what amount a chemical species may be present, which comprises

- (a) depositing on a substrate (i) a pair of interdigitated electrodes each having a comb-like configuration and (ii) in such manner that the electrodes are electrically connected, a thin film of a multiplicity of particles having a core of conductive metal or conductive metal alloy, in each said particle the core being from 0.8 to 40.0 nm in maximum dimension, and deposited on said core a ligand shell, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered; and
- (b) connecting said pair of electrodes with a sensor capable of determining a change in the property of said multiplicity of particles.

28. A method of fabrication as defined in claim 27, wherein said deposition of a thin film of the multiplicity of particles comprises spraying on the electrodes and on the substrate a solution comprising a salt of each conductive metal to be incorporated in said core, an organic substance having a functional group which is capable of interacting with said species, and a solvent for each said salt and said substance, said electrodes being at a temperature such that the solvent is flashed away.

29. A method of fabrication as defined in claim 27, wherein said deposition of a thin film of the multiplicity of particles comprises

- (a) treating said electrodes and substrate with a difunctional material capable of binding with (i) the electrodes and the substrate and (ii) said multiplicity of said particles, such that said material binds with said electrodes and said substrate;
- (b) contacting the treated electrodes and substrate with said multiplicity of particles having a core of conductive metal or conductive metal alloy, in each said particle the core being from 0.8 to 40.0 nm in maximum dimension, and deposited on said core a ligand shell, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that

a property of said multiplicity of particles is altered, such that said multiplicity of particles bonds with the material to form a composite comprising a layer of said particles on the electrodes and substrate.

30. A method of fabrication as defined in claim 29, wherein the multiplicity of particles forms a monolayer on said substrate and electrodes.

31. A method of fabrication as defined in claim 27, which further comprises a cycle of steps including

(a) exposing the outwardly facing surfaces of said particles of the composite to a coupling agent capable of bonding said particles to a further multiplicity of such particles deposited thereon, the particles of said further multiplicity having a core of conductive metal or conductive metal alloy, in each said particle the core being from 0.8 to 40.0 nm in maximum dimension, and deposited on said core a ligand shell, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered; and

(b) contacting the particle surfaces so exposed with said further multiplicity of particles such that said further multiplicity of particles bonds with the particle surfaces of said composite, and the further multiplicity of particles is immobilized on those surfaces.

32. A method of fabrication as defined in claim 31, wherein said cycle is performed a plurality of times.

33. A system suitable for investigating a target environment to determine whether or in what amount a chemical species may be present, which comprises

(a) a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8

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to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered;

(b) means for exposing said multiplicity of particles to said environment;

(c) means for subjecting said multiplicity of particles to conditions sufficient for said property to be exhibited; and

(d) means for monitoring said property to determine whether there is, or the amount of, any change in such property as an indication of whether or in what amount said species is present.

34. A system for investigating a target environment to determine whether or in what amount a chemical species may be present, which comprises

(a) a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that the electrical resistivity of said multiplicity of particles is altered;

(b) means for exposing said multiplicity of particles to said environment;

(c) means for passing an electrical current through said multiplicity of particles; and

(d) means for monitoring the electrical resistivity of said multiplicity of particles to determine whether there is, or the amount of, any change in said resistivity as an indication of whether or in what amount said species is present.

35. A system as defined in claim 34, wherein said means for monitoring the electrical resistivity of said multiplicity of particles includes a current-to-voltage converter circuit followed by a precision rectifier and low-pass filter.

36. A system as defined in claim 35, wherein said means further includes a voltage-to-frequency converter.